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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,553	05/02/2002	Audrey Goddard	P3230R1C001-168	9988

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EXAMINER	
KOLKER, DANIEL E	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 07/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,553	GODDARD ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,7,9 and 11-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,7,9 and 11-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/17/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's remarks filed 17 April 2006 have been entered. Claims 1 – 5, 8 and 10 are canceled. Claims 6 – 7, 9, and 11 – 17 are pending and under examination.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Continued Examination Under 37 CFR 1.114

3. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 April 2006 has been entered.

Status of Previously Submitted Amendments

4. Applicant states, on p. 4 of the remarks filed 17 April 2006, that no communication had been received as to the status of the after-final amendment mailed 10 March 2006. This communication was received by the USPTO and granted the filing date of 14 March 2006. The amendment was entered, and an advisory action was mailed to applicant on 28 March 2006. A copy of the advisory action was mailed to:

Knobbe Martens
2040 Main St., Fourteenth Floor
Irvine CA 92614

This is the address of record for this application. Should there be an error in this address, applicant is requested to correct it so that future correspondence is received. In any case, the advisory action can be viewed on the USPTO's Public PAIR website at http://portal.uspto.gov/external/portal/pair

Withdrawn Rejections and Objections

5. The following rejections and objections made in the previous office action are withdrawn:

A. The rejection of claims 12 – 13 under 35 USC 112, first paragraph for lack of written description is withdrawn in light of the arguments. However note the rejection of claims 14 – 17 is maintained.

Maintained Rejections and Objections

Priority

6. The effective filing date for all pending claims is 24 August 2000. Applicant did not traverse this statement and thus the examiner's determination stands for the reasons of record.

Claim Rejections - 35 USC §§ 101 and 112

7. Claims 6 – 7, 9, and 11 – 17 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

This rejection is maintained for the reasons of record. Briefly, the claims encompass proteins at least 95% identical to SEQ ID NO:48 as well as certain fragments and variants. The specification discloses that a small undisclosed stretch of SEQ ID NO:47 (about 200 – 600 bp, see p. 140 paragraph 0530), a nucleic acid which encodes to SEQ ID NO:48, is expressed more highly in normal stomach than stomach tumor, and more highly in rectum tumor than in normal rectum. There are no data presented as to whether the protein (SEQ ID NO:48, also called PRO994) is differentially expressed in any tumor, nor is there evidence of the utility of the protein for diagnosis or treatment of any disease. Applicant argues extensively that the disclosure of data on nucleic acids is sufficient to confer utility on the claimed proteins, but provides no evidence as to the over- or under-expression of the in any disease or condition, and also provides no evidence that the proteins can be used for treatment or diagnosis.

Applicant argues, beginning on p. 5 of the remarks filed 17 April 2006, that the PTO has failed to adequately support the utility rejection. Applicant argues that she may substitute a reasonable correlation between evidence presented and an asserted utility in place of direct evidence on whether or not the claimed invention is useful. In this case, applicant is presenting data on the nucleic acid, PRO994 mRNA, and attempting to correlate that expression with the expression of PRO994 protein, which is claimed herein.

Applicant argues that the examiner's reliance on the article by Hu et al. is inappropriate for two reasons: 1) Hu only presents data from published literature results and is not a

systematic survey of gene expression – protein expression correlations and 2) Hu et al. discuss microarray data, whereas in the instant case Example 18 is a PCR-based assay, not a microarray. The source of Hu's data are not particularly relevant to the validity and applicability to the instant case. Whether the data were pulled from existing articles or from a *de novo* experiment is not germane to the question of whether mRNA levels correlate with protein levels. Applicant also argues that the abstract by Kuo et al. teaches that there is a good correlation between mRNA and protein levels, when RT-PCR is used. Applicant provided only the abstract by Kuo; the examiner has obtained the entire article and is enclosing it herein. Kuo et al. (2005 Proteomics 5:894-906) clearly teach that the amount of mRNA and protein determined to be in a sample is highly technique-dependent. See for example p. 904, first column, where they discuss microarray data in fact correlate well with Western blot data, but not 2-D gel data, and guide the artisan to take care in determining which isoforms of a protein are present in a sample when making such correlations. In the instant case, applicant has not determined which isoforms are present in any protein samples. In fact, applicant has only presented data on nucleic acid, not protein. Thus because applicant has clearly not followed the guidance of Kuo, it is difficult to see how the article supports the position that mRNA in a nucleic acid sample is predictive of protein levels.

Applicant also argues (p. 7) that the Tokunaga reference is not sufficient to support the position that considerable further research is necessary to use the claimed invention in diagnosis of cancer. Applicant's arguments have been fully considered but they are not persuasive. Tokunaga does indeed discuss some of the difficulties in using absolute mRNA levels as diagnostics, but also points out the many problems with RT-PCR as a method. See particularly Tokunaga, p. 380 first column, where the authors discuss how this method, the same one used by the instant applicants in Example 18, leads to false-positives, as well as detection below the level of physiological relevance. Tokunaga et al. suggest particular modifications to the RT-PCR method including use of internal controls, to prevent such problems, but applicant did not undertake any such precautions. Importantly, there is no evidence that the levels of mRNA detected by applicant are even physiologically relevant when elevated.

Beginning on p. 8, applicant argues that changes in mRNA levels are generally predictive of protein levels and offers the analogy between the nucleic acid protein situation and a car's ability to travel greater distances on greater amounts of gas. Applicant argues that

because in some circumstances an increase in mRNA level leads to an increase in protein levels, the examiner should concede that the situation is more likely true than not in the instant case (see p. 9 of the remarks). However, the reference already of record by Chen clearly shows that one cannot make this conclusion.

Applicants further contend that the limited teachings in Chen that do address changes in mRNA level support corresponding changes in the level of encoded protein. Specifically, Applicants argue that Figures 2A-2C show a correlation between mRNA/protein pairs for three specific genes, and that this supports Applicants' assertion of a correlation between mRNA and protein changes in general.

Applicant's arguments have been fully considered but are not found to be persuasive. The results in Chen shown in Figure 2A-2C represent three examples wherein protein levels were correlated with mRNA (out of 17 identified). Chen found 137 protein spots wherein protein levels were not correlated with mRNA levels. However, Chen does not report the individual variation within any of these samples (which included normal tissue and tumor tissue). Therefore, these samples may or may not have included mRNA and/or protein levels that were differentially expressed. Chen simply does not provide enough information to address the issue whether changes in mRNA levels generally result in similar changes in protein levels. All that Chen clearly teaches is that mRNA levels do not predict protein levels, as they disclose at pg 304 that "[t]he use of mRNA expression patterns by themselves, however, is insufficient for understanding the expression of protein products, as additional post-transcriptional mechanisms, including protein translation, post-translational modification, and degradation, may influence the level of a protein present in a given cell or tissue" (see pg 304, right column).

Chen found only 17% of the genes examined had significant correlations between mRNA and protein levels (p. 311, first column). This is very clear evidence that it is not proper to conclude that there is a general correlation between mRNA and protein levels. It is particularly relevant that both Chen et al. and the instant application are dealing with samples from cancerous tissues, which quite frequently experience genetic dysregulation. Such problems can cause, for example, an overexpression at the nucleic acid level which can be compensated for post-transcriptionally or even post-translationally. Thus when looking at cancerous tissue, it is clearly not appropriate to conclude that the changes in nucleic acid expression are representative of changes in protein expression. In the instant case data have been provided only on nucleic acid expression, but the claims are drawn to proteins.

Beginning on p. 11 of the remarks, applicant discusses references by Ortonft, Wang, Munaut, Hui, Khal, Maruyama, Caberlotto, Misrachi, Stein, and Guo, which applicant argues should be able to substitute for actual evidence on the claimed invention. It is important to note that none of these references, or the references cited beginning on p. 15 (i.e. Futcher, Godbout, Papotti, Van der Wilt, Grenback, Shen and Fu, or in fact any of the 113 references cited on pp. 15 – 17 of the remarks) are on point to whether or not expression of the claimed proteins, i.e. those at least 95% identical to SEQ ID NO:48, are correlated with expression of the nucleic acid that encodes it. Except for the Orntoft reference each of the references submitted by Applicants is directed to a single gene, or a small number of genes. These references are consistent with Chen who found 17% of proteins do show correlation between mRNA and protein, and the examples of these proteins in Chen that show that changes in mRNA correlate with changes in protein level. However, these studies examining the expression of small numbers of genes are not found persuasive in view of comprehensive studies where significantly larger numbers of transcripts and proteins were examined, specifically, Nagaraja (2006), Waghray (2001) and Sagynaliev (2006) which are described below.

With regard to the Orntoft reference, Applicants submit that Orntoft examined 40 well-resolved abundant proteins, and found significant correlation between mRNA and protein alterations (including both increases and decreases) for each gene, except one.

Applicants' arguments with respect to Orntoft have been fully considered but are not found to be persuasive. Orntoft compared the mRNA and proteins levels of about 40 well-resolved and focused abundant proteins with known chromosomal locations. The instant specification does not teach whether or not PRO994 is a "well focused abundant" protein with a known chromosomal location as characterized by Orntoft. Furthermore, other relevant publications (Nagaraja (2006), Waghray (2001), and Sagynaliev (2005)) report that increases in mRNA and protein samples are not correlated (see below).

The Examiner maintains the previous argument that mRNA levels are not necessarily predictive of protein levels, and in response to Applicants' arguments, maintains that this is true even when there is a changes in the mRNA level. Comprehensive studies comparing changes in expression of the transcriptome and proteome support this argument. Nagaraja (2006) teaches, "We have characterized comprehensive transcript and proteomic profiles of cell lines corresponding to normal breast (MCF10A), noninvasive breast cancer (MCF7) and invasive breast cancer (MDS-MB-231)...the proteomic profiles indicated altered abundance of few

proteins as compared to transcript profiles" (See abstract of Nagaraja, 2006, Oncogene. 25: 2328-2338). Nagaraja further teaches, "The comparison of transcript profiles with proteomic profiles demonstrated that altered proteins were not always represented in the microarray designated profiles and *vice versa*" (pg 2329) and "As dictated by post-transcriptional regulation, protein profiles showed far fewer changes as compared to transcript profiles" (pg 2335).

Similarly, Waghray (2001) teaches, "we have analyzed gene expression changes induced by dihydrotestosterone (DHT) in the androgen responsive cancer line LNCaP, at both RNA and protein levels" (see Abstract of Waghray, 2001. Proteomics. 1: 1327-1338). Waghray identified transcripts from 16570 genes and found "351 genes were significantly altered by DHT treatment at the RNA level." Waghray identified 1031 protein and found 44 protein spots that changed in intensity (either increased or decreased). Twenty-nine of these proteins were identified and "remarkably, for most of the proteins identified, there was no appreciable concordant change at the RNA level (Table 4)" If changes in protein generally reflected mRNA changes, based on the fact that 2% of the genes analyzed had a change in transcript levels (351 out of 16570 genes), one would expect at least 2% of protein levels to change, or 22 out of 1031 protein spots. Therefore, it is significant that while the authors found 44 proteins that did change, very few of the identified ones had a similar change in mRNA expression.

In a review of gene expression in colorectal cancer (CRC), Sagynaliev (2006) teaches, "One thousand two-hundred and forty genes have been reported to be dysregulated (up- and/or down-regulated) in human CRC, representing about 5% of the 20000-25000 human genes" (pg 3067). Sagynaliev also teaches, "a total of 408 proteins were found to be differentially expressed in human CRC in at least one study" and importantly, "It is also difficult to reproduce transcriptomics results with proteomics tools. Out of 982 genes found to be differentially expressed in human CRC by genome-wide transcriptomics technologies (Table 6a), only 177 (18%) have been confirmed using proteomics technologies" (pg 3068).

In summary, it is clear that Nagaraja, Waghray and Sagynaliev support that changes in mRNA expression frequently does not result in changes in protein expression. Therefore, the Examiner maintains that Applicants' measurement of an increase of PRO994 mRNA does not provide a specific and substantial utility for the encoded protein. Applicant has submitted several references showing that in some cases, there is a correlation between mRNA expression and the expression of the encoded protein. The PTO has provided many references that indicate that this correlation is hardly universal and that underscore the conclusion that it is

improper to correlate nucleic acid and protein expression data, particularly in the case of cancerous tissue samples. Thus the state of the art of mRNA-protein expression correlations is quite clearly unpredictable. In some cases, there may be correlations, but in other cases there are not likely to be correlations. No clear generalizations can be made as to whether the expression of a protein product will change when the expression of a nucleic acid that encodes said protein changes. Applicant's assertion that it is more likely than not true that there is such a correlation is not borne out by the evidence of record. For these reasons, the rejection under 35 USC § 101 is maintained.

8. Claims 6 – 7, 9, and 11 – 17 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9. Even if utility were found for the polypeptide of SEQ ID NO:48, claims 6, 9, 12 – 17 would remain rejected under 35 USC § 112, first paragraph because the specification does not reasonably provide enablement for polypeptides which either consist of, or alternatively comprise, residues 32 – 49 or 111-190 of SEQ ID NO:48, or for variants at least 95% identical to SEQ ID NO:48 which can make antibodies used to detect the full-length protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

In the instant case, the nature of the invention is complex. The claims are broad in that they encompass proteins including residues 32-49 or 111-190 of SEQ ID NO:48, as well as variants which fusion proteins, as well as variants related by sequence identity to full-length

SEQ ID NO:48, which have the ability to make an antibody. The specification discloses that a certain undisclosed nucleic acid that encodes a part of PRO994 is expressed more highly in normal stomach than stomach tumor, and more highly in rectum tumor than in normal rectum. The specification does not disclose if either the section of the protein recited in claim 6, part(b), or in claim 9, or in claim 14, part(b) is encoded by the nucleic acid. The specification does not disclose whether these small fragments, or any protein comprising them, is in fact over- or under-expressed in any tumor. The specification does not teach the artisan how to use either of these fragments, or how to use variants at least 95% identical to them, or how to use chimeric proteins comprising them, or how to use any polypeptide comprising them. There is no disclosure of how to use the full genus, or even a reasonable number of members of the genus, of proteins which comprise these fragments. There is only disclosure of a single member falling within the scope of the genus, namely full-length SEQ ID NO:48. Even assuming, for the sake of argument alone, that the full-length protein is useful, there is no disclosure in either the specification or in the prior art of record, for any use for the fragments which include residues 32-49 or 111-190 of SEQ ID NO:48.

Claims 14 – 17 require that the protein variant be able to produce an antibody which is useful for detecting SEQ ID NO:48. Hopp et al. (1981. Proc Natl Acad Sci USA 78:3824-3828, cited in previous office action) teach that as few as six amino acids are sufficient to make an antibody. Claims 14 – 17 do not require that any particular structure be present, nor do the claims teach the artisan which regions are sufficient to make an antibody, or which ones are necessary to ensure that the antibody will "specifically detect the polypeptide of SEQ ID NO:48" as recited in claims 14 and 15. For an antibody to "specifically detect" a protein means that it will not detect other proteins, thus ensuring to the artisan who uses it that the target protein in question (here, SEQ ID NO:48) is what is actually identified by the antibody. The specification does not teach the artisan which regions of SEQ ID NO:48 are required so that the resultant antibody will have the required specificity.

Thus given the breadth of the claims, in that they encompass far more than what is actually disclosed, the lack of working examples, or even of prophetic examples, of how to use residues 32-49 or 111-190 of SEQ ID NO:48, the lack of guidance in the specification as to which regions of SEQ ID NO:48 or of those small fragments (i.e. residues 32-49 or 111-190) are either necessary or sufficient to make the antibodies with the specificity recited in claims 14 and

15, it would take undue experimentation for the artisan to both make and use the invention commensurate in scope with the claims.

10. Claims 14 – 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

This rejection is maintained for the reasons of record and explained in further detail here. Briefly, the claims are drawn to polypeptides at least 95% identical to SEQ ID NO:48, or to residues 32-49 or 111-190 of SEQ ID NO:48, wherein the resultant protein can make an antibody to specifically detect SEQ ID NO:48. The specification discloses only a single member of the broad genus, namely SEQ ID NO:48 itself. The examiner concedes that making variants is within the skill of the artisan, and testing antibodies is within the skill of the artisan. However, whether or not the artisan is so skilled does not indicate that the specification discloses that applicant was in possession of the claimed invention.

As discussed previously, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Applicant again points the examiner to Example 14 of the written description training materials as providing support for the argument that claims to proteins at least 95% identical to the disclosed sequence with an appropriate functional limitation are deemed to meet the description requirement. In that case, the relevant functional activity which is specific to that protein is recited in the claim, namely the catalytic activity of the enzyme. In the instant case, the only activity that is recited in claims 14 – 15 is the ability to make an antibody. Every protein of at least six amino acids in length is able to make an antibody. Thus reciting this activity in the body of the claim does not make the situation analogous to Example 14 of the written description training materials.

Applicant is again directed to the flow chart on p. 9 of the Revised Written Description Interim Guidelines Training Materials, available on the internet at <http://www.uspto.gov/web/offices/pac/writtendesc.pdf>, which is analogous to the instant situation. Claims 14 – 17 are genus claims. Because the recite percentage identity, the necessarily encompass more than one member of the genus. The specification only discloses a single member of the genus, namely SEQ ID NO:48. The specification does not disclose which residues are required for the so-called functional activity recited in claims 14 and 15, the ability to make an antibody which can detect SEQ ID NO:48. There is no disclosure of whether or not residues 32-49 or 111-190 of SEQ ID NO:48 will make antibodies with this specificity, or whether said antibodies will cross-react with other proteins. There is no disclosure of the structural features which are common to all members of the genus encompassed by claims 14 – 15, and therefore by dependent claims 16 – 17 as well.

Applicant also argues, beginning on p. 21 of the remarks, that the recent CAFC decision *In re Wallach* indicates that one can be in possession of an entire genus merely by describing a single member of that genus. Applicant's arguments have been fully considered but they are not persuasive. In *Wallach*, the court stated that if a protein is fully described by its amino acid sequence, the entire genus of nucleic acids which encode that protein can be considered described as well. Since the genetic code is so well-known that one of ordinary skill in the art would immediately be able envision all the possible permutations of nucleic acid sequences which encode that protein. In fact, the genetic code is routinely published in textbooks, so one would only have to consult a table to determine which nucleic acid codons relate to each disclosed amino acid.

The examiner concedes that the court's reasoning here is exactly correct. However, it is not relevant to the instant fact pattern and the court ruled that in spite of this the specification in *Wallach* did not provide an adequate written description of the claimed invention. In the instant case, applicant is not attempting to claim a genus of nucleic acids based on the disclosure of a single amino acid. Rather, in claims 14 – 17, applicant claims to have been in possession of the full genus of proteins at least 95% identical (claim 14) or 99% identical (claim 15) to SEQ ID NO:48 which have the functional property of being able to produce an antibody which detects SEQ ID NO:48. The specification does not disclose which structural elements are required or are sufficient to imbue the protein with that function. It does not disclose to the artisan how to distinguish that genus of proteins from those proteins 95% or 99% identical to SEQ ID NO:48

but which do not have this property.

In *Wallach*, the Federal Circuit in fact upheld the examiner's conclusion, and the board's affirmation of that conclusion, that the specification which disclosed isolation of a protein on an SDS-PAGE gel, as well as certain in vitro properties of the protein and the sequence of ten amino acids at N-terminus, did not in fact show that the appellant was in possession of the genus of nucleic acids which encode that protein. The court cited the previous decision in Amgen v. Chugai, stating that

> "[c]onception does not occur *unless one has a mental picture of the structure of the chemical*, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. *It is not sufficient to define it solely by its principal biological property*, ... because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property." (citations deleted; ellipsis in original text from *Wallach*, emphasis added).

Thus in *Wallach*, the court found that the specification failed to provide a sufficient written description of the claimed chemical invention, because it did not disclose those features which distinguish the genus of claimed compounds. On p. 22 of the remarks, applicant argues that the facts in the instant case are very close to those in *Wallach*. To the extent that that is true, it would tend to support the examiner's rejection for lack of written description, as the court ruled in *Wallach* that the examiner and the Board of Patent Appeals and Interferences were both correct in their conclusions that the specification did not describe the claimed invention.

11. Claims 6, 9, 12 – 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 6, 9, and 14 – 17 each encompass polypeptides comprising amino acid sequences selected from residues 32-49 and 111-190 of SEQ ID NO:48, or polypeptides at least 95% identical thereto, or chimeric proteins comprising same. The examiner is unable to find support for proteins comprising these regions in the specification as originally filed. There is

support chimeric molecules comprising full-length PRO polypeptides, for example at p. 10 paragraph [0023]. Figure 48 discloses transmembrane domains at residues 10-31, 50-72, 87-110, and 191-213 for only the polypeptide of SEQ ID NO:48. Residues 32-49 and 111-190 are between these domains. However the examiner is unable to find disclosure of the following claimed products in the originally-field application:

A) generic polypeptides merely comprising residues 32-49 or 111-190 of SEQ ID NO:48, as recited in claim 6, part (b) and claim 9

B) polypeptides at least 95% identical to residues 32-49 or 111-190 of SEQ ID NO:48, as recited in claim 14, part(b) and claim 15, part(b).

C) chimeric proteins comprising either A) or B) above, as claimed in claims 12 – 13 and 16 – 17.

As the originally-filed disclosure does not describe that applicant was in possession of the invention now claimed, these claims are rejected for reciting new matter.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Daniel E. Kolker, Ph.D.
June 16, 2006

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER